

Laryngeal Chondrosarcomas: The Mayo Clinic Experience

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Background: Laryngeal chondrosarcomas occur infrequently. Their management is often guided by inferences made from the management of sarcomas arising from more commonly afflicted organs.

Method: A retrospective analysis of patients with laryngeal chondrosarcomas treated at the Mayo Clinic between 1959 and 1992 was performed to assess prognostic factors and outcomes after various treatments.

Results: A total of 20 patients received treatment during this time period. All chondrosarcomas were low grade; 19 involved the cricoid cartilage and one arose in the supraglottic larynx. Initial treatment consisted of local excision (often subtotal removal) alone in 12 patients (60%), hemilaryngectomy in 2 (10%), near total laryngectomy in 2 (10%), and total laryngectomy in 4 (20%). Six patients (30%) had local recurrence: five initially had local excision and one had hemilaryngectomy. All local recurrences or tumor progression developed >3 years after initial treatment. Salvage surgery was performed in five of the six patients who had local recurrence, and the other patient was observed. Of the five patients who had salvage surgery, three required another resection because of a second recurrence.

Conclusions: These results suggest that initial conservative subtotal laryngectomy should be explored further because this treatment may provide long-term voice preservation in most patients, and patients who experience a recurrence after local excision often have been given several years of voice preservation. *J. Surg. Oncol.* 1997;65:269–273. © 1997 Wiley-Liss, Inc.

KEY WORDS: larynx; recurrence; chondrosarcoma

INTRODUCTION

Laryngeal chondrosarcomas account for <1% of all sarcomas. Approximately 250–300 cases have been reported in the literature [1,2]. Chondrosarcomas comprise the majority of laryngeal sarcomas [3,4]; however, sarcomas of various histologic patterns have been reported to arise in the larynx [3,5–7]. Before the routine use of modern immunohistologic classification methods, it was difficult to characterize these tumors fully.

Because most physicians and most medical centers rarely encounter a patient with laryngeal chondrosar-

coma, the management of patients with these tumors has often been guided by inferences made from the management of sarcomas arising in more commonly afflicted organs [8–14]. This report reviews our institutional experience with laryngeal chondrosarcomas for the years 1959–1992, following a modern appraisal of all patho-

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logic specimens. This analysis was performed to assess the natural history and response to treatment of laryngeal chondrosarcomas.

MATERIALS AND METHODS

Patients

A retrospective analysis was performed of all patients with laryngeal chondrosarcomas evaluated at the Mayo Clinic between January 1959 and December 1992. Approximately 9,262 patients with sarcomas were identified; of these, 28 underwent evaluation or received therapy (or both) for laryngeal sarcoma at the Mayo Clinic. The pathologic diagnosis was established using standard histologic criteria in interpreting hematoxylin-eosin-stained preparations [15]. The diagnosis was supported by immunohistochemical studies of tissue (available for 27 of 28 specimens). These immunohistochemical studies included antibodies to keratin, antibodies to leukocyte common antigen, muscle stains (actin, desmin, and myoglobin), and the S-100 protein stain. All specimens were reviewed by one pathologist (J.E.L.). Of the 28 laryngeal sarcomas, 20 were chondrosarcomas and form the basis of this report. No patient had a history of previous laryngeal irradiation.

During the years encompassed by this study, the initial workup varied greatly for patients with laryngeal chondrosarcomas and frequently was confined to examination, chest radiography, and biopsy. During the 1960s and early 1970s, computed tomographic (CT) evaluation of the neck was not available. This procedure was used more commonly in the later half (1980s) of the study. Of the 20 patients with chondrosarcomas, 19 had chest X-rays and 8 had CT of the neck.

Treatment and Assessment of Failures

Surgical excision was the primary treatment for the 20 patients (local excision in 12, hemilaryngectomy in 2, near-total laryngectomy in 2, and total laryngectomy in 4). Patterns of treatment failure were assessed. Local recurrence was defined as recurrence in the laryngeal region (supraglottic, glottic, or subglottic); regional recurrence as failure in lymph nodes adjacent to the original site of the laryngeal sarcoma; and distant recurrence as metastases outside the confines of the above definitions. Also, time to local recurrence was calculated (i.e., time from date of initial diagnosis to date of local recurrence).

Statistical Analysis

For the 20 chondrosarcoma patients, statistical analyses were performed to determine the prognostic significance of initial type of treatment with respect to local recurrence. Curves summarizing time to local recurrence by initial type of treatment were calculated and plotted using the product-limit method of Kaplan and Meier

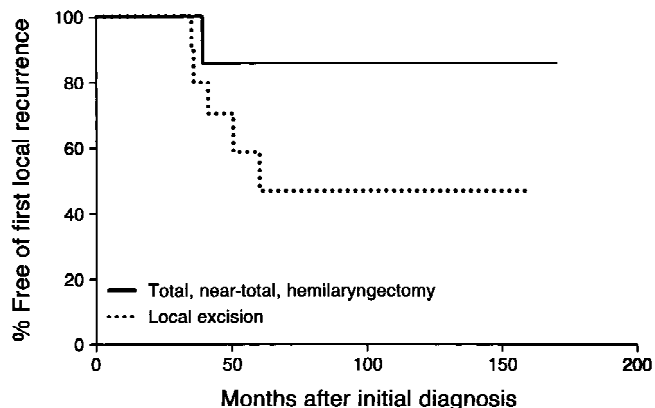


Fig. 1. Patients with laryngeal chondrosarcomas who initially had local excision had a suggestion of decreased local control compared with patients receiving more extensive procedures. Failure-free survival (all failures were local recurrences) is represented as time after diagnosis.

Total log-rank $P = 0.14$	First		
	N	recurrence	Median
	8	1	NA
	12	5	61
	20	6	

[16]. The log-rank test was used to compare differences between these curves [17]. Fisher's exact test [18] was used to compare differences in patient characteristics by local recurrence status among the group of 12 chondrosarcoma patients who were initially treated with local excision.

RESULTS

Patient Characteristics

Among the 17 of 20 patients with chondrosarcoma who were alive, the mean (median) follow-up time was 94 (93) months. Follow-up information was obtained from clinic history notes, or it was supplied by the patient through the Mayo Cancer Registry. Twenty patients had chondrosarcomas; all were low grade (grade 1 or 2) tumors. Of these 20 patients, 19 had tumors that involved the cricoid; the other tumor arose in the supraglottic larynx. The initial treatment for all 20 patients was surgery alone and included local excision (usually subtotal removal) in 12, hemilaryngectomy in 2, near-total laryngectomy in 2, and total laryngectomy in 4. There were 16 males and 4 females. The median age was 65 years (47–83).

It was difficult retrospectively to assess the bulk of these lesions, and it was not possible to assess the criteria used for the selection of the various surgical procedures. In general, patients (6/8) with tumors >3 cm in diameter were more likely to have an extensive surgical procedure (hemilaryngectomy, near-total laryngectomy, or total laryngectomy) because of involvement of the cricoid and airway compromise. Figure 1 shows a comparison of

TABLE 1. Characteristics of 12 Patients With Chondrosarcomas Treated With Initial Local Excision

Characteristic	Local control (n = 7)	Local recurrence ^a (n = 5)
Age, yr		
Mean	64	68
Range	47–73	61–83
Sex, no.		
Male	6	3
Female	1	2
Size of tumor, no.		
≤3 cm	4	3
>3 cm	3	2
Grade, no.		
I	7	4
II	0	1
Presenting with stridor/difficulty breathing/choking/dysphagia*		
Yes	1	4
No	6	1

^aAll recurrences were local; no regional or distant metastases were noted.

*Exact *P* value corresponding to 1/7 vs. 4/5 is 0.07.

time to recurrence among patients with chondrosarcomas by initial treatment. There was a suggestion that patients who had more extensive surgical treatment (hemilaryngectomy or near-total or total laryngectomy) had a lower incidence of recurrence than those who had local excision alone ($P = 0.14$). However, all recurrences developed >3 years postoperatively. These results illustrated the extended length of time that the voice is preserved after local excision, even for patients who eventually develop a local recurrence requiring a more extensive procedure.

Local excision was the initial surgical intervention in 12 patients, and Table I lists the general characteristics of these patients with respect to whether the patients' tumors were controlled locally or not. Age, sex, and size and grade of the tumor were not significantly different between patients in whom local control was achieved and those who had local recurrence. When the presenting symptoms of stridor, difficulty breathing, choking, and dysphagia were considered together, there was suggestion of a trend that such symptoms were more common in patients who had a local recurrence (4/5 patients vs. 1/7 patients, $P = 0.07$ [exact χ^2]). Because tumor bulk was not easy to assess retrospectively, these symptoms may merely identify patients with greater tumor bulk.

For the entire group of chondrosarcomas, six patients had local recurrence or tumor progression requiring further treatment: in five after local excision and in one after hemilaryngectomy. A plot of time from first to second local recurrence for this group of six patients is shown in Figure 2. The observed local control rate was 75% at 2 years and 25% at 5 years after first local recurrence. The complete management of these six patients is outlined in

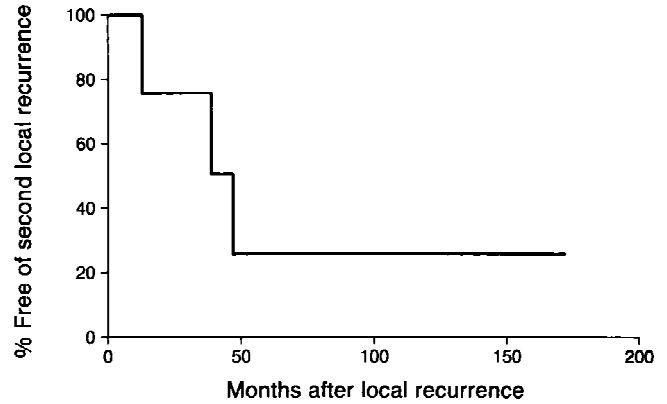


Fig. 2. Risk of second treatment failure (all failures were local recurrences) after salvage surgery for initial failure in patients with laryngeal chondrosarcomas.

N	Second recurrence	Median
6	3	39

TABLE II. Treatment of Six Patients With Chondrosarcoma Who Had Local Recurrence After Initial Treatment

Patient	Initial treatment ^a	Time to recurrence (mos.)	Treatment of recurrence ^b	Status ^c
1	LE	36	Observation	AWD
2	LE	42	LE	AWD
3	LE	51	LE	AWD
4	LE	61	TL	NED
5	LE	37	LE	NED
6	HL	39	TL	NED

^aLE = local excision; HL = hemilaryngectomy.

^bLE = local excision; TL = total laryngectomy.

^cAWD = alive with disease; NED = no evidence of disease.

Table II. No patient in this group developed metastatic disease. These results suggest that local excision is an important treatment modality for providing several years of voice preservation, because tumor dedifferentiation or the development of metastatic disease did not occur, even for the patients who developed a local recurrence.

DISCUSSION

Most of the sarcomatous tumors found in the larynx are chondrosarcomas, as corroborated by this series (20 of 28 patients). These laryngeal chondrosarcomas are generally low grade [15] and do not metastasize, as indicated by the current series. Dedifferentiation with associated metastasis has been reported to occur in rare cases [19], but this was not seen in the current series.

Generally, the initial treatment of chondrosarcomas has consisted of surgical removal of the tumor. If possible, excision with preservation of most laryngeal functions is attempted, because these tumors have a low

TABLE III. Failure Patterns for Laryngeal Chondrosarcomas

Author ^a	Year	No. of patients	Treatment (no. of patients) ^b	All recurrences ^c	Local control ^d
Goethals et al. [20]	1963	18	LE (16) TL (2)	6/16 0/2	10/16 2/2
Putney and Moran [21]	1964	2	LE (2)	2/2	0/2
Barsocchini and McCoy [22]	1968	3	LE (2) TL (1)	2/2 0/1	0/2 1/1
					1/1 (F/U 4 mo)
Huizenga and Balogh [23]	1970	8	LE (5) TL (2) RT (1)	5/5 0/2 1/1	0/5 2/2 0/1
al-Saleem et al. [24]	1970	10	LE (8) TL (2)	5/8 1/2 (D)	3/8 One patient lost to F/U
Ostberg et al. [25]	1979	6	LE (6)	4/6	2/6
Gorenstein et al. [6]	1980	7	LE (3) TL (3)	1/3 0/3	2/3 3/3
			Tracheostomy only (1)	—	—
Neel and Unni [26]	1982	31	LE (19) TL (7)	6/19 0/7	13/19 7/7
			External removal (3)	0/3	3/3
			Tracheostomy only (2)	—	—
Ferlito et al. [3]	1984	3	LE (1) TL + RT (1)	1/1 1/1 (D,L)	0/1 0/1
			SL (1)	0/1	1/1
Lavertu and Tucker [27]	1984	1	STL (1)	1/1	0/1
Kambic et al. [9]	1989	1	LE (1)	1/1	0/1
Hakky et al. [28]	1989	1	LE (1) TL (1)	1/1 0/1	0/1 1/1
Neis et al. [2]	1989	2	LE (1) TL (1)	0/1 0/1	1/1 1/1
Nicolai et al. [29]	1990	8	LE (2) TL (3)	2/2 0/3	0/2 3/3 (1 with F/U 2 mo)
			LE + RT (1)	0/1	1/1
			TL + RT (1)	1/1 (D,L)	0/1
			SL (1)	0/1	1/1
Brandwein et al. [19]	1992	11	LE (9) TL (2)	3/9 0/2	6/9 2/2
Kozelsky et al. (present study)	1996	20	LE (12) TL, HL, NTL (8)	5/12 1/8	7/12 7/8
Total		91 ^e	LE (66) TL (25)	36/66 (54.5%) 4/25 (16.0%)	30/66 (45.5%) 21/25 (84.0%)

^aReference number in brackets.^bLE = local excision (includes partial laryngectomy and laryngofissure, thyrotomy with excision); TL = total laryngectomy; RT = radiation therapy; SL = supraglottic laryngectomy; STL = subtotal laryngectomy; HL = hemilaryngectomy; NTL = near-total lumpectomy.^cD = distant; L = local.^dF/U = follow-up.^eDoes not include studies by Gorenstein et al. [6], Neel and Unni [26], and Ferlito et al. [3]; patients in these studies are included in the more recent studies of Nicolai et al. [29] and Kozelsky et al.

metastatic potential and minimizing the morbidity of treatment is an important goal. As expected, there was a suggestion that local recurrences were more frequent (Fig. 1, $P = 0.14$) in patients whose initial treatment was local excision alone (subtotal removal) (5-year local control = 58%) than in those who had a more extensive procedure (5-year local control = 86%). However, the patients who had initial local excision often were provided with voice preservation for the remainder of their

lives or for many years (all >3 years in this series). The above finding was corroborated by a compilation of all available studies that included information on failure patterns (Table III). This compilation [2,3,6,9,19–29] revealed that ~55% of patients who initially had local excision had local recurrences, whereas local recurrence developed in only 16% of patients who initially had total laryngectomy (Table III). In the current study, an effort was made to identify patients at greatest risk for local

recurrence after local excision because they may be an appropriate group in which to study the use of a surgical adjuvant treatment. The current review pointed to a possible population for this type of study in that it suggested that tumor recurrence or symptomatic disease progression after an initial excision may have been more common in patients who presented with symptoms of stridor, difficulty breathing, choking, or dysphagia, i.e., larger tumors. Although patients were provided additional time with voice preservation after a second attempt at conservative surgery, long-term local control was difficult to achieve with further conservative salvage surgery. The observed local control rate was 75% at 2 years and 25% at 5 years (Fig. 2). These patients often eventually required a laryngectomy (five of six patients in the present series).

The suggestion of a greater rate of local recurrence after local excision alone than after more extensive procedures is not unexpected, because many chondrosarcomas arise in the cricoid (19 of 20 in the present series) and preservation of the larynx and airway may involve the use of piecemeal removal of tumor or curettage of the tumor bed and the margins of resection may be minimal. It is possible that technical advances in these surgical procedures may improve the rate of local control with surgery alone. Another possible avenue of investigation for patients who undergo local excision with minimal or no margin of resection would be the use of postoperative radiation therapy. Although chondrosarcomas traditionally have been considered radioresistant tumors, several investigators have shown promising results with the use of radiation in these tumors [30,31]. Harwood et al. [30] demonstrated that ~50% of patients with primary chondrosarcomas of bone that were treated primarily with radiation achieved durable complete responses (3–16 years of follow-up). Future clinical research protocols should consider the use of adjuvant radiotherapy after conservative surgery in an attempt to obviate re-resection (and possibly several future recurrences) of these tumors. To date, however, only a few case reports exist pertaining to the use of radiation for these patients. For instance, Tran et al. [7] treated two patients with radiation after resection with positive margins; neither patient developed a recurrence, but the follow-up time was not specified. Further work is necessary to better define the role of any adjuvant therapy.

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